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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/805,177	03/14/2001	Richard Bruce Roden	031787.0090	2532

21967 7590 03/08/2004

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EXAMINER	
RAWLINGS, STEPHEN L	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 03/08/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/805,177	RODEN ET AL.	
	Examiner	Art Unit	
	Stephen L. Rawlings, Ph.D.	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 September 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-45* is/are pending in the application.

4a) Of the above claim(s) *1-40 and 42-45* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *41* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. The amendment filed September 15, 2003 is acknowledged and has been entered. Claims 1, 2, 5, 9, 10, 12, 15, 17, 18, 30, 41, 42, 43, and 45 have been amended.

2. Claims 1-45 are pending in the application. Claims 1-40 and 42-45 have been withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim.

3. Claim 41, insofar as the claim is drawn to a method for screening for cancer comprising determining the presence of antibodies specific for ATP-dependent iron transporter ABC-7, is currently under prosecution.

Drawings

4. The proposed substitute drawing filed September 15, 2003 is acknowledged. As Applicant has stated amended Figure 12 contains the same content as that of originally filed Figure 12, albeit it is differently formatted, the proposed substitute drawing is acceptable.

Election/Restrictions

5. Applicant's remarks regarding the restriction at page 18 of the Amendment filed September 15, 2003 are acknowledged. However, Applicant's interpretation that claim 41 is a generic claim, or has been treated as a generic claim and that the currently prosecuted invention of screening for cancer comprising detecting antibodies to ATP-dependent iron transport ABC-7 protein amounts to an election of species is inaccurate. The Examiner set forth in Paper Nos. 9 and 11 that claim 41 encompasses distinct inventions, not distinct species. The Examiner does not consider claim 41 to be a generic claim, because the instantly recited Markush group is improper, as its members are not interrelated by a common feature. Although Applicant asserts claim 41 is

generic, Applicant has not pointed to any generic feature common to each member of the Markush group. Because the instantly recited Markush group contains no common, unifying feature applicable to each member of the group, claim 41 cannot be examined as a generic claim. Accordingly, the members of the Markush group are not sufficiently few in number or so closely related that a search and examination of the entire claim can be made without serious burden. Consideration of each member of the Markush group would require a separate search, as the search required to consider one is not co-extensive with the search required to consider any other, and although members of the Markush group may be few, it is proper to restrict members of the Markush group, where the members represent independent or distinct inventions and where the members either do not share a common utility or do not share a substantial feature disclosed as being essential to that utility. Therefore, to the extents that claim 41 is drawn to each different member of the Markush group, claim 41 is viewed as encompassing independent or distinct inventions, not different species of a generic invention. See MPEP § 803.02.

The restriction is deemed proper and is made FINAL.

Grounds of Objection and Rejection Withdrawn

6. Unless specifically reiterated below, the grounds of objection and rejection set forth in the previous Office action mailed March 14, 2003 have been withdrawn.

Specification

7. The specification is objected to because the use of numerous improperly demarcated trademarks has been noted in this application. Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner that might adversely affect their validity as trademarks. See MPEP § 608.01(v).

An example of an improperly demarcated trademark includes American Type Culture Collection™ at page 22.

Appropriate corrections are required. Each letter of a trademark should be capitalized or otherwise the trademark should be demarcated with the appropriate symbol indicating its proprietary nature (e.g., ™, ®), and accompanied by generic terminology. Applicants may identify trademarks using the "Trademark" search engine under "USPTO Search Collections" on the Internet at http://www.uspto.gov/web/menu/search.html.

Claim Objections

8. Claim 41 is objected to because the claim is alternatively drawn to the subject matter of non-elected inventions.

Claim Rejections - 35 USC § 112

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claim 41 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

As stated in the previous Office action, even given the benefit of Applicant's disclosure, one skilled in the art could not have a reasonable expectation of successfully practicing the claimed invention to assess the likelihood that an individual has cancer without need of performing additional and an undue amount of experimentation. For the reasons set forth therein, given the state of the art and the high level of unpredictability associated therewith, the amount of guidance, direction, and exemplification would be insufficient to enable the use of the claimed invention as required by 35 USC § 112, first paragraph.

Applicant has traversed this ground of rejection arguing the following:

(a) The teachings of Gadduci et al., Creaney et al., and Mack et al. are not relevant, as the instant claims are drawn to a method for screening ovarian cancer comprising determining the presence of antibodies that bind ABC-7, whereas Gadduci et al., Creaney et al., and Mack et al. present findings that the presence of p53 autoantibodies lacks prognositic and diagnostic value.

(b) Specifically regarding Gadducci et al., Applicant argues the reference is irrelevant because Gadducci et al. teaches the presence of p53 autoantibodies has no prognostic value, whereas claim 41 is drawn to a diagnostic method.

(c) Regarding the teachings of Tockman et al., Applicant argues a showing of such magnitude, i.e., a validation of the value of a biomarker against acknowledged disease end points, is not required to satisfy the requirements set forth under 35 USC §§ 101 and 112, first paragraph. Applicant argues that based upon the disclosure, the skilled artisan would more likely than not conclude the invention can be practiced in a manner that might provide immediate benefit to the public without need of first performing an undue amount of experimentation.

(d) Applicant has argued given the benefit of the disclosure, the skilled artisan could practice the claimed invention with a reasonable expectation of success without need to first perform an undue amount of experimentation. Applicant has asserted the disclosure provides ample guidance, direction, and exemplification to enable the successful application of the claimed method. Applicant further asserts only routine experimentation, and not an undue amount, would be needed to practice the claimed invention successfully.

Applicant's arguments have been carefully considered but not found persuasive for the following reasons:

(a) In reply to Applicant's argument the teachings of Gadduci et al., Creaney et al., and Mack et al. are not relevant, as the instant claims are drawn to a method for screening ovarian cancer, claim 41 is not so limited. Claim 41 is presently drawn to a method for screening for cancer, not ovarian cancer *per se*. Furthermore, the teachings of Gadduci et al., Creaney et al., and Mack et al. are indeed relevant, as the references

are analogous, establish the state of the art, and show the level of unpredictability that is associated therewith.

(b) In reply to Applicant's argument the teachings of Gadduci et al. are not relevant, because Gadducci et al. teaches the presence of p53 autoantibodies has no prognostic value, whereas claim 41 is drawn to a diagnostic method, the Examiner disagrees. It is well understood in the art that some markers are better suited as diagnostic markers, while others are better used as prognostically. Nevertheless, just as the teachings of Gadducci et al. indicate p53 autoantibodies cannot be used to assess an individual's prognosis, the teachings also suggest that the skilled artisan would not accept the assertion that the presence of autoantibodies against ABC-7 is indicative of cancer, absent a showing otherwise, because one skilled in the art cannot predict whether the mere presence of autoantibodies can be used to assess the likelihood that an individual will be found to have cancer. As further evidence of this fact and as noted in the previous Office action, Creaney et al. teaches autoantibodies may not serve as diagnostic markers of cancer. Because it is well known in the art that the detection of some tumor markers has proven to be ineffective in enabling an accurate diagnosis of cancer in a subject, the skilled artisan cannot predict whether the claimed invention can be used to screen for cancer and therefore the skilled artisan could not practice the claimed invention without need of performing additional and an undue amount of experimentation.

(c) Regarding Applicant's arguments concerning the relevancy of the teachings of Tockman et al. and Applicant's assertion the invention can be successfully practiced as disclosed without need of performing an undue amount of experimentation, the preponderance of evidence suggests otherwise. Factors to be considered in determining whether undue experimentation is required are summarized in *Ex parte Forman*, 230 USPQ 546 (BPAI 1986). These factors include the nature of the invention, the state of the prior art, the relative skill of those in the art, the amount of direction or guidance disclosed in the specification, the presence or absence of working examples, the predictability or unpredictability of the art, the breadth of the claims, and the quantity of experimentation which would be required in order to practice the invention as

claimed. Careful consideration of these factors in view of the teachings of Creaney et al., Mack et al., Gadducci et al., and Tockman et al. indicates even given the benefit of Applicant's disclosure, one skilled in the art could not have a reasonable expectation of successfully practicing the claimed invention to assess the likelihood that an individual has cancer without need of performing additional and an undue amount of experimentation.

(d) At pages 22 and 23 of the Amendment, Applicant has argued given the benefit of the disclosure, the skilled artisan could practice the claimed invention with a reasonable expectation of success without need to first perform an undue amount of experimentation. Applicant has asserted the disclosure provides ample guidance, direction, and exemplification to enable the successful application of the claimed method. Applicant further asserts only routine experimentation, and not an undue amount, would be needed to practice the claimed invention successfully. In reply, the application of the claimed method is not exemplified in the disclosure. The examples to which Applicant refers do not set forth guidance and direction for practicing the claimed invention; the examples merely illustrate the methodology Applicant practiced in making the discovery that one cDNA clone encoding an antigen to which one patient's immune serum reacts encodes the ABC-7 polypeptide. The disclosed examples do not remedy the deficiency, which is evident in view of the teachings of Creaney et al., Mack et al., Gadducci et al., and Tockman et al., namely that the success of practicing the claimed invention cannot be predicted, such that one skilled in the art would have a reasonable expectation of success in practicing the claimed invention to screen for cancer without having the need to first perform an additional and undue amount of experimentation.

Finally, in reply to Applicant's argument only routine experimentation need be practiced to have a reasonable expectation of success, it is again duly noted at page 4, the specification discloses: "[T]he clinical significance of detection of autologous anti-tumor antibodies requires further analysis and must be assessed for each antigen". The need to first assess the clinical significance of the presence of the autoantibodies constitutes more than a mere need to perform routine experimentation to, for example, optimize the method, but rather constitutes an undue amount of experimentation,

especially since the likelihood that the presence of the autoantibody will be found clinically significant cannot be predicted.

11. Claim 41 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

As stated in the previous Office action, claim 41 is interpreted as a method for screening for cancer comprising determining the presence of antibodies that bind specifically to a genus of proteins collectively designated "ATP-dependent iron transporter ABC-7", which includes isoforms and variants of the protein having the GenBank™ accession number AF133659. However, because the specification only sets forth an adequate description of a single member of the genus of proteins, namely the protein having the GenBank™ accession number AF133659, the written description is deemed insufficient to meet the written description requirements set forth under 35 USC § 112, first paragraph.

Applicant has traversed this ground of rejection arguing Applicant has clearly identified "ABC-7" as GenBank™ Accession No. AF133659, such that the claim only encompasses a method comprising determining the presence of antibodies that bind specifically to the protein having the sequence set forth as GenBank™ Accession No. AF133659, but to no other protein. Accordingly, Applicant argues the written description of the claimed invention is sufficient to meet the requirements set forth under 35 USC § 112, first paragraph.

Applicant's arguments have been carefully considered but not found persuasive for the following reasons:

At page 34 the specification teaches that an isolated nucleic acid molecule encoding a protein that is specifically reactive with the immune serum of a patient diagnosed with ovarian cancer is "the ABC-7 ATP-dependent iron transporter (**consistent** with the sequence of gb|AF133659|AF133659)" (emphasis added).

Therefore, the "ATP-dependent iron transporter ABC-7" to which claim 41 is drawn is merely described as having an amino acid sequence consistent with the sequence disclosed as GenBank™ accession number AF133659. Therefore, as explained in the previous Office action, the claim encompasses a method comprising determining the presence of antibodies that bind any protein designated as "ATP-dependent iron transporter ABC-7", including the isoforms or variants of the protein described by Allikmets et al., which have not been described in the specification. For example, it appears claim 41 encompasses a method comprising determining the presence of antibodies specific the protein of GenBank™ accession number BC006323, which is defined as human ATP-binding cassette, sub-family B (MDR/TAP), member 7 (ABC-7). GenBank™ accession number BC006323 is 99.4% identical to the polynucleotide sequence of GenBank™ accession number AF133659. While the former protein appears to be a member of the genus of ATP-dependent iron transporter ABC-7 proteins to which the claims are drawn, the former protein is not described in the specification.

12. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

13. Claim 41 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

As stated in the previous Office action, claim 41 is vague and indefinite because the claim recites the term "increased likelihood". The metes and bounds of the invention cannot be reasonably determined, as it cannot be ascertained what probability constitutes "an increased likelihood".

Applicant has traversed this ground of rejection arguing, as read in light of the specification, one skilled in the art would readily understand what is meant by the term "increased likelihood". Applicant argues the mere use of terms of degree, such as "increased likelihood, does not render the claim *per se* indefinite.

Applicant's arguments have been carefully considered but not found persuasive for the following reasons:

In reply to Applicant's argument the mere use of terms of degree, such as "increased likelihood, does not render the claim *per se* indefinite, because it cannot be determined relative to what standard the comparison is to be made, the skilled artisan would not readily understand the term "increased likelihood".

Conclusion

14. Claim 41 is not allowed.

15. The prior art made of record and not relied upon is considered pertinent to Applicant's disclosure. Gottschlich et al., Hogdall et al., and Lee et al. teach autoantibodies cannot be used to screen for cancer. Ward et al. and US Patent No. 5,356,817 A teach not all markers can be used reliably in diagnosis of all types or stages of cancer.

16. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stephen L. Rawlings, Ph.D. whose telephone number is

(571) 272-0836. The examiner can normally be reached on Monday-Friday, 8:30AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne L. Eyler, Ph.D. can be reached on (571) 272-0871. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Stephen L. Rawlings, Ph.D.
Examiner
Art Unit 1642

slr
February 25, 2004

YVONNE EYLER, PH.D
SUPERVISORY PATENT EXAMINER
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